MedAdapter: Efficient Test-Time Adaptation of Large Language Models Towards Medical Reasoning

Wenqi Shi[♠*], **Ran Xu**[♡*], **Yuchen Zhuang**[♠], **Yue Yu**[♠], **Haotian Sun**[♠], **Hang Wu**[♠], **Carl Yang**[♡], **May D. Wang**[♠]

♠ Georgia Tech ♡ Emory University
{wqshi,yczhuang,yueyu,haotian.sun,hangwu,maywang}@gatech.edu
{ran.xu,j.carlyang}@emory.edu

Abstract

Despite their improved capabilities in generation and reasoning, adapting large language models (LLMs) to the biomedical domain remains challenging due to their immense size and privacy concerns. In this study, we propose MedAdapter[1], a unified post-hoc adapter for test-time adaptation of LLMs towards biomedical applications. Instead of fine-tuning the entire LLM, MedAdapter effectively adapts the original model by fine-tuning only a small BERT-sized adapter to rank candidate solutions generated by LLMs. Experiments on four biomedical tasks across eight datasets demonstrate that MedAdapter effectively adapts both white-box and black-box LLMs in biomedical reasoning, achieving average performance improvements of 18.24% and 10.96%, respectively, without requiring extensive computational resources or sharing data with third parties. MedAdapter also yields enhanced performance when combined with train-time adaptation, highlighting a flexible and complementary solution to existing adaptation methods. Faced with the challenges of balancing model performance, computational resources, and data privacy, MedAdapter provides an efficient, privacy-preserving, cost-effective, and transparent solution for adapting LLMs to the biomedical domain.

1 Introduction

Large language models (LLMs) (OpenAI, 2022, 2023; Team et al., 2023) have demonstrated superior generation and reasoning capabilities compared to traditional BERT-sized language models, primarily due to the massive number of parameters and extensive pre-training on vast textual corpora. In the biomedical domain, researchers have developed LLMs that are either pre-trained (Chen et al., 2023b; Bolton et al., 2024a) or fine-tuned (Singhal et al., 2023; Han et al., 2023) on large-scale domain-specific corpora to enhance performance on biomedical natural language processing (NLP) tasks. However, tuning biomedical domain-specific LLMs triggers additional considerations due to their *immense size* and *corporate privacy*, especially given (1) the **resource constraints** in academic institutions and medical centers and (2) the **sensitive nature** of clinical data.

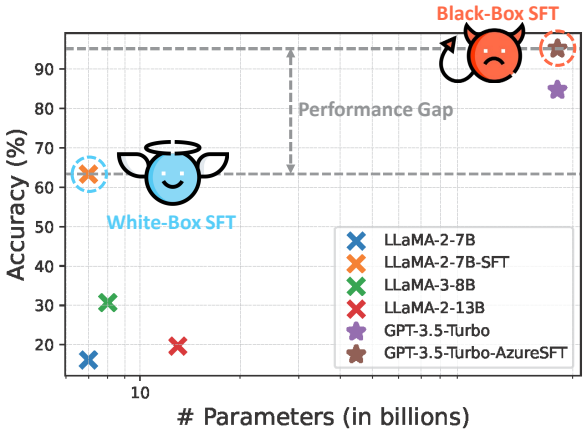

Figure 1: Evaluation results on BioASQ. X-axis in log scale. Moderately-sized white-box LLMs consistently *underperform* larger black-box LLMs, regardless of fine-tuning on biomedical corpora. However, fine-tuning black-box LLMs through APIs can pose potential *data privacy risks* and incur *substantial costs*.

Although fine-tuning LLMs accelerates biomedical discovery and improves patient care (Han et al., 2023; Zhang et al., 2023; Wang et al., 2024), it usually necessitates complete access to internal parameters, which is currently limited to white-box LLMs like LLaMA-series models (Touvron et al., 2023; Meta-AI, 2024). However, a significant *performance discrepancy* still exists between larger black-box LLMs (*e.g.*, GPT-3.5-Turbo) and smaller white-box LLMs (*e.g.*, LLaMA-2) (Labrak et al., 2024; Singhal et al., 2023; Chen et al., 2023b), even when

[*] Equal contribution.
[1] Our implementation of MedAdapter is available at https://github.com/wshi83/MedAdapter.

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the latter are fine-tuned on biomedical-specific corpora (Figure 1). Moreover, fine-tuning even a moderately-sized LLM with 7B parameters requires *substantial computational resources* (Bolton et al., 2024a), often exceeding the capabilities of many academic and medical centers.

Such intrinsic limitations of white-box LLMs intuitively motivate the exploration of adapting black-box LLMs to the biomedical domain. While it is possible to fine-tune black-box LLMs like GPT-3.5 (OpenAI, 2022) via third-party APIs (Peng et al., 2023) without direct access to internal parameters, this approach presents several unique challenges within the field of biomedicine: (1) Uploading patient data via APIs poses significant risks of *privacy leakage* and potential conflicts with Health Insurance Portability and Accountability Act (HIPAA) compliance, including unauthorized third-party access to personally identifiable information (PII) (Lukas et al., 2023; Marks and Haupt, 2023; Wang et al., 2023a); (2) Fine-tuning API services could incur prohibitively *high financial and environmental costs* (Luccioni et al., 2023), exceeding typical academic or clinical budgets; (3) The opaque fine-tuning process, limited to very few adjustable hyperparameters within a specific range, often results in *suboptimal performance* in downstream tasks (Sun et al., 2024), whereas medical applications often demand precise outcomes.

In this study, we rethink the trade-off between model performance concerns in white-box LLMs and data privacy issues in black-box LLMs for biomedical tasks from a new perspective. We introduce `MedAdapter`, a unified test-time adapter that fine-tunes **a lightweight BERT-sized language model (110M)** to facilitate the adaptation of both white-box and black-box LLMs for medical reasoning. Instead of updating the parameter for the entire LLM, `MedAdapter` fine-tunes a small outcome-supervised adapter that ranks candidate solutions generated by LLMs, effectively and efficiently adapting the original LLM to the target domain. In addition, it also eliminates the need to (1) access the large-scale internal model parameters or (2) share any private patient information with third parties through fine-tuning APIs.

Extensive experiments on **four biomedical reasoning tasks across eight datasets** demonstrate that `MedAdapter` effectively adapts both white-box and black-box LLMs for medical reasoning, achieving average performance improvements of 18.24% and 10.96%, respectively. *For white-box LLMs*, `MedAdapter` reaches 99.35% of supervised fine-tuning performance using only 14.75% of the GPU memory on BioASQ. *For black-box LLMs*, it achieves comparable performance or even surpasses fine-tuning APIs at only 15.59% of the budget, while also eliminating the risks associated with private data sharing. We summarize our contributions as follows:

- We introduce `MedAdapter`, a **unified** post-hoc adapter designed to facilitate the efficient test-time adaptation of both white-box and black-box LLMs for medical reasoning.
- Compared to supervised fine-tuning of white-box LLMs, `MedAdapter` achieves **effective** domain adaptation using a **BERT-sized** language model with only 110M parameters.
- Compared to supervised fine-tuning of black-box LLMs via APIs, `MedAdapter` offers a more **privacy-preserving**, **cost-efficient**, and **transparent** alternative, eliminating the need for access to any model parameters.
- When combined with train-time adaptation, `MedAdapter` outperforms either train-time or test-time adaptation alone, underscoring its utility as a **flexible** and **complementary** solution to existing adaptation methods.

2 `MedAdapter`: Adapting LLMs to Medical Reasoning

2.1 Preliminaries

Problem Formulation. Test-time adaptation[2] refers to the process of customizing models to test data that may exhibit distributional deviations from the original training data. Given a pre-trained LLM G_ϕ and a training dataset from the target domain $\mathcal{D} = \{(\mathbf{x}_i, \mathbf{y}_i)\}_{i=1}^{|\mathcal{D}|}$, where $\mathbf{x}_i$ typically describes the task input and $\mathbf{y}_i$ represents the ground-truth answer for the i-th example. The goal is to adapt the outputs of the LLM $\hat{\mathbf{y}}_i^s \in \mathcal{Y}^S$ from the general source domain to a specific target domain $\mathbf{y}^t \in \mathcal{Y}^T$ for each input instance $\mathbf{x}_i$. Such adaptation can be crucial for enhancing the capability of an LLM to exhibit biomedical domain-specific reasoning,

[2]We adopt a slightly different definition of test-time adaptation than several existing studies (Zancato et al., 2023; Karmanov et al., 2024); we only require target domain label information to remain invisible to the original LLM and stay accessible to the adapter.

which may be underdeveloped in its original outputs. According to the accessibility of model parameters, existing approaches can be categorized into two main groups: (1) *white-box* LLM adaptation, which allows full access to model parameters, and (2) *black-box* LLM adaptation, which permits no such access.

White-box LLM Adaptation. With model parameters available in white-box LLMs, the most direct approach for domain adaptation is supervised fine-tuning (Wei et al., 2022a; Chung et al., 2024) with the negative log-likelihood learning objective on the training data:

$$\mathcal{L}_{\text{SFT}}(\phi) = -\mathbb{E}_{(\mathbf{x},\mathbf{y})\sim\mathcal{D}} \sum_{t=1}^{T} \log G_\phi(\mathbf{y}_t|\mathbf{y}_{<t}, \mathbf{x}). \tag{1}$$

In practice, for efficient adaptation of large pre-trained models to various downstream applications, parameter-efficient fine-tuning (PEFT) methods (Houlsby et al., 2019; Hu et al., 2022) have been proposed. These methods involve fine-tuning only a small subset of (additional) model parameters, significantly reducing both computational and storage costs. Although PEFT-based methods provide a practical solution with limited computational resources, they compromise model performance for efficiency.

Black-box LLM Adaptation. State-of-the-art LLMs, including GPT-4 (OpenAI, 2023), Claude (Anthropic, 2024), and Gemini (Team et al., 2023), adhere to a trend of non-disclosure of model parameters to the public. Consequently, fine-tuning these black-box LLMs relies solely on fine-tuning web service APIs, such as the OpenAI GPT-3.5-turbo fine-tuning API (Peng et al., 2023), which lacks transparency and incurs high costs. In response, recent black-box adaptation methods (Liu et al., 2024; Ormazabal et al., 2023; Huang et al., 2023) have explored the adjustment of logit biases for increasing the frequency of tokens from the target domain appearing in the output while penalizing those from the source domain. However, such black-box adaptation methods remain inapplicable to the latest cutting-edge black-box LLMs, such as GPT-3.5-turbo (OpenAI, 2022), due to the *unavailability of token probabilities*. Although few recent studies (Xu et al., 2023; Sun et al., 2024) bypass the need for full parameter access, they are *limited to specific tasks*: they only support classification tasks that rely on label predictions with confidence (Xu et al., 2023), or multi-step reasoning tasks that require process-level supervision and beam search (Sun et al., 2024). These constraints significantly limit the applicability of such methods to diverse biomedical reasoning applications.

2.2 Overview of `MedAdapter`

The rapid increase in the size of LLMs exacerbates the existing disparity between resource-abundant and resource-scarce biomedical institutions (Gema et al., 2023), especially given the high privacy of patient information. To address this, we propose `MedAdapter`, a unified post-hoc adapter that facilitates test-time adaptation without the need for significant computational resources or access to model parameters (Figure 2). Benefiting from the strong generation capabilities of recent LLMs, we first leverage LLMs to generate candidate reasoning solutions (Section 2.3). We then fine-tune a BERT-sized language model, `MedAdapter`, to rank all candidate solutions, thereby establishing the distinction between the source and target domains (Section 2.4). Finally, `MedAdapter` adapts LLMs by sampling the candidate solution with the highest adaptation score (Section 2.5).

2.3 Candidate Solutions Generation

For each problem $\mathbf{x}_i$ in the training dataset $\mathcal{D}$, we generate k intermediate candidate reasoning solutions $\{\hat{\mathbf{s}}_{i,j}\}_{j=1}^{k}$ (*e.g.*, chain-of-thought rationales or multi-step reasonings) and the corresponding answer $\{\hat{\mathbf{y}}_{i,j}\}_{j=1}^{k}$ using greedy decoding with the language model generator G. With access to ground-truth answers $\mathbf{y}_i$, we can verify the correctness of each generated solution $\hat{\mathbf{y}}_{i,j}$ and assign a corresponding binary correctness label z_i as:

$$z_i = \mathbb{1}(\hat{\mathbf{y}}_{i,j} = \mathbf{y}_i),\ z_i \in \{0, 1\}. \tag{2}$$

With the generated solutions, we formulate a new dataset for the adapter training, denoted as:

$$\mathcal{D}_{\text{ada}} = \{(\mathbf{h}_{i,j}, z_i) \mid 1 \le i \le |\mathcal{D}|, 1 \le j \le k\}, \tag{3}$$

where $\mathbf{h}_{i,j} = [\mathbf{x}_i||\hat{\mathbf{s}}_{i,j}||\hat{\mathbf{y}}_{i,j}]$, represents the concatenation of the medical question and the entire candidate generation, and z_i is a binary label indicating whether $\hat{\mathbf{y}}_{i,j}$ is a correct or incorrect solution.

2.4 Outcome-Supervised Adapter

To enable the distinction between source and target domain, we train an outcome-supervised adapter (*i.e.*, verifier) that assesses the probability of correctness for a candidate solution relative to a given

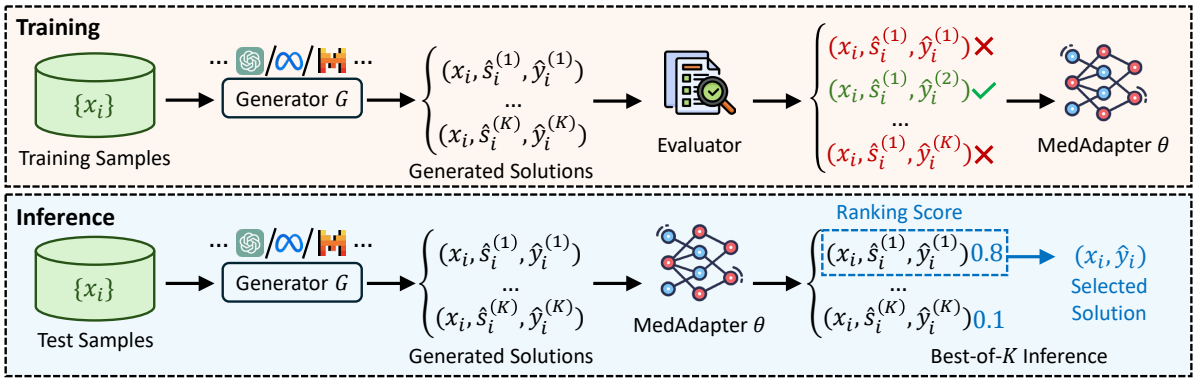

Figure 2: Overview of MedAdapter for efficient test-time LLM adaptation towards medical reasoning. We fine-tune a small adapter, MedAdapter, to rank candidate solutions generated by LLMs, thereby effectively establishing a distinction between the source and target domains for efficient domain adaptation.

problem. During inference, the language model G generates a set of candidate solutions, and the one ranked highest by the verifier is selected as the final answer, aligning closely with the target domain. More specifically, given a medical reasoning problem $\mathbf{x}$ and its corresponding candidate solutions $\hat{\mathbf{y}}$, the outcome verifier ($V : \mathcal{X} \times \mathcal{Y} \rightarrow \mathbb{R}$) assigns a normalized adaptation score, ranging from 0 to 1, to each solution to indicate the correctness.

In MedAdapter, we fine-tune a BERT-sized language model θ ($\sim$ 110M parameters), to function as an outcome-supervised adapter on $\mathcal{D}_{\text{ada}}$. Following the empirical study on the effect of different objective functions in Section 3.7, we employ a combination of language modeling and binary classification as the objective function:

$$\mathcal{L}_{\text{ada}} = z \log V_\theta(\mathbf{h}) + (1 - z) \log(1 - V_\theta(\mathbf{h})), \tag{4}$$

where z is the binary label verified against the ground-truth answer provided in $\mathcal{D}_{\text{ada}}$, and $V_\theta(\mathbf{h})$ is the sigmoid adaptation score of the question-solution pair $\mathbf{h}$ assigned by the adapter model.

2.5 Best-of-K Inference

During the inference stage, for each test question $\mathbf{x}_i$, we adopt the best-of-K inference, often referred to as rejection sampling, to select the best solution from multiple candidates. We initially sample K candidate solutions $\{\hat{\mathbf{s}}_{i,j}, \hat{\mathbf{y}}_{i,j}\}_{j=1}^{K}$ from the generator G. The solution with the highest adaptation score is then selected:

$$\hat{\mathbf{y}}_i = \arg \max_{j=1,\cdots,K} r_\theta([\mathbf{x}_i || \hat{\mathbf{s}}_{i,j} || \hat{\mathbf{y}}_{i,j}]). \tag{5}$$

Remark. We note that, in contrast to prior verification-guided in-context learning methods (Li et al., 2023a; Khalifa et al., 2023) that depend on large-scale intermediate reasoning annotations, MedAdapter utilizes candidate solutions generated by LLMs to form positive and negative examples, thus removing the need for human-annotated intermediate reasoning steps. Additionally, the lightweight design of the adapter θ results in a minimal increase in memory usage and inference time. The efficiency study is presented in Section 3.5.

3 Experiments

3.1 Experimental Setups

Tasks and Datasets. For a comprehensive evaluation, we examine MedAdapter mainly on five datasets for biomedical QA task: (1) **MedMCQA** (Pal et al., 2022), (2) **MedQA** (Jin et al., 2021), (3) **MMLU** (Hendrycks et al., 2021), (4) **PubMedQA** (Jin et al., 2019), (5) **BioASQ** (Tsatsaronis et al., 2015); and three additional biomedical NLP tasks, including (6) **MedNLI** (Shivade, 2017) for natural language inference (NLI), (7) **MediQA-RQE** (Ben Abacha et al., 2019) for recognizing question entailment (RQE), and (8) **PubHealth** (Kotonya and Toni, 2020) for health fact-checking. For detailed information, please refer to Appendix A.

Baselines. We conduct our main experiments using both white-box and black-box backbone LLMs. We employ the *Chain-of-Thoughts* (CoT) results (Wei et al., 2022b) as the baseline performance for all backbone LLMs without adaptation.
◇ For white-box LLM adaptation, we primarily compare MedAdapter against *supervised fine-tuning*, which updates all of the model parameters and serves as the upper-performance benchmark. We adapt widely used open-source LLaMA mod-

Dataset (→)	MedMCQA		MedQA		MMLU-Med		PubMedQA		BioASQ		MedNLI		MediQA-RQE		PubHealth	
Method (↓)/Metrics (→)	Acc. (%)	Δ (%)	Acc. (%)	Δ (%)	Acc. (%)	Δ (%)	Acc. (%)	Δ (%)	Acc. (%)	Δ (%)	Acc. (%)	Δ (%)	Acc. (%)	Δ (%)	Acc. (%)	Δ (%)
LLaMA-2-7B (2023)	16.00	–	16.42	–	20.13	–	17.00	–	16.13	–	17.80	–	23.91	–	16.89	–
+Self-Consistency (2023b)	21.20	+5.20	22.39	+ 5.97	23.27	+3.14	28.00	+11.00	17.74	+1.61	27.87	+10.07	25.22	+1.31	17.79	+0.90
+MedAdapter	32.00	+16.00	32.52	+16.10	27.67	+7.54	58.00	+41.00	62.90	+46.77	30.46	+12.66	27.39	+3.48	19.25	+2.36
+SFT†	42.86	+26.86	33.39	+16.97	28.22	+8.09	60.80	+43.80	63.31	+47.18	65.52	+47.72	35.42	+11.51	22.00	+5.11
BioMistral-7B (2024)	28.95	–	29.77	–	33.33	–	26.20	–	28.53	–	22.03	–	42.37	–	25.73	–
+Self-Consistency (2023b)	29.18	+0.23	32.68	+2.91	39.62	+6.29	30.60	+4.40	31.45	+2.92	31.46	+9.43	44.68	+2.31	28.90	+2.17
+MedAdapter	30.31	+1.36	34.88	+5.11	46.54	+13.21	33.20	+7.00	33.06	+4.53	35.96	+13.93	45.53	+3.18	30.84	+5.11
LLaMA-3-8B (2024)	20.44	–	27.81	–	25.16	–	19.00	–	30.65	–	21.96	–	49.13	–	27.70	–
+Self-Consistency (2023b)	26.87	+6.43	31.50	+3.69	31.45	+6.29	37.00	+18.00	33.06	+2.41	30.12	+8.16	50.87	+1.74	35.01	+7.31
+MedAdapter	32.08	+11.64	32.44	+4.63	35.22	+10.06	55.00	+36.00	64.52	+31.46	32.09	+10.13	51.74	+2.61	36.07	+8.37
LLaMA-2-13B (2023)	19.66	–	28.04	–	22.01	–	47.40	–	19.66	–	21.75	–	30.44	–	19.33	–
+Self-Consistency (2023b)	28.40	+ 8.74	31.03	+2.99	28.30	+ 6.29	56.80	+9.40	51.61	+31.95	24.21	+2.46	43.04	+12.60	24.70	+5.37
+MedAdapter	32.00	+12.34	37.47	+9.43	33.96	+11.95	63.60	+16.20	65.32	+45.66	26.88	+5.13	44.78	+14.34	27.46	+8.13
gpt-3.5-turbo (2022)	49.74	–	61.51	–	59.75	–	56.00	–	84.68	–	66.64	–	50.00	–	23.38	–
+Self-Consistency (2023b)	56.20	+6.46	67.71	+6.20	69.81	+10.06	71.60	+15.60	87.90	+3.22	69.18	+2.54	51.30	+1.30	25.41	+2.03
+MedRAG (2024)	51.80	+2.06	64.36	+2.85	68.85	+9.10	50.00	-6.00	87.55	+2.87	–	–	–	–	–	–
+MedAdapter	59.02	+9.28	68.66	+7.15	73.58	+13.83	73.40	+17.40	93.55	+8.87	75.09	+8.45	52.61	+2.61	33.43	+10.05
+Azure-SFT† (2023)	61.82	+12.08	63.32	+1.81	70.55	+10.80	71.40	+15.40	95.16	+10.48	91.27	+24.63	58.08	+8.08	36.56	+13.18
gpt-4 (2023)	69.48	–	83.90	–	85.53	–	69.20	–	92.74	–	86.77	–	51.30	–	38.52	–
+Self-Consistency (2023b)	70.08	+0.60	84.05	+0.15	86.79	+1.26	72.20	+3.00	93.54	+0.8	87.26	+0.49	51.74	+0.44	43.35	+4.83
+MedRAG (2024)	66.65	-2.83	82.80	-1.10	87.24	+1.71	70.60	-1.40	92.56	-0.18	–	–	–	–	–	–
+MedAdapter	72.09	+2.61	84.13	+0.23	87.42	+1.89	77.40	+8.20	95.97	+3.23	87.68	+0.91	53.04	+1.74	46.34	+7.82

Table 1: Main results (accuracy) of adapting white-box and black-box LLMs to biomedical tasks. † denotes the upper bound in theory using supervised fine-tuning (SFT). Specifically, we perform Azure-SFT for black-box LLMs via Microsoft Azure OpenAI fine-tuning API services to ensure compliance with HIPAA regulations. Notations are consistent across tables. The results of MedRAG on smaller LLMs are not reported in their paper.

els (Touvron et al., 2023; Meta-AI, 2024) across various versions and scales, as well as medical domain-specific LLMs like BioMistral-7B (Labrak et al., 2024) for a comprehensive evaluation.

◇ For black-box LLM adaptation, we focus on the comparison between MedAdapter and *supervised fine-tuning* using the Microsoft Azure OpenAI fine-tuning API service (Peng et al., 2023). In addition, we compare MedAdapter with other privacy-preserving solutions, including *self-consistency* (Wang et al., 2023b) and medical domain-specific *retrieval-augmented generation* (RAG) (Xiong et al., 2024), which do not require uploading training data to third parties[3].

Evaluation Metric. Following Bolton et al. (2024a), we adopt accuracy as the main evaluation metric for all biomedical tasks.

Implementation Details. In this work, we employ LongFormer-Base (110M) (Beltagy et al., 2020) as the base language model for MedAdapter. We set $k = 8$ for all generations of intermediate candidate reasoning solutions using MedAdapter. Additional implementation details, including prompt templates, are available in Appendix B.

[3]We incorporate in-context learning baselines in biomedical applications from privacy-preserving perspectives. Note that due to context length limits, in-context learning can only rely on a limited number of supervised examples; the model performance is only for reference.

3.2 Main Results

In Table 1, we summarize the experimental results of adapting both white-box and black-box LLMs for four biomedical tasks across eight datasets.

White-box LLM Adaptation. ◇ Effectiveness: Across all downstream biomedical applications, MedAdapter consistently outperforms the original white-box LLM, LLaMA-2-7B (Touvron et al., 2023), with an average performance improvement of 25.48% for QA task, 12.66% for NLI, 3.48% for RQE, and 2.36% for fact-checking, respectively, demonstrating the adaptability of MedAdapter towards diverse biomedical domain-specific applications. ◇ Efficiency: Notably, MedAdapter demonstrates its efficiency by achieving 87.50% of the performance level of the fully supervised fine-tuning model while only updating an adapter comprising 110M parameters, which constitutes merely 1.57% of the parameters (7B) of the original model. ◇ Robustness: It also demonstrates an average improvement of 13.34% over another lightweight test-time adaptation solution, self-consistency (Wang et al., 2023b), with more robust adaptation across all tasks. ◇ Generalization: Additionally, MedAdapter further improves the performance of domain-specific LLMs like BioMistral-7B (Labrak et al., 2024) and general-domain LLMs at different scales, such as LLaMA-3-8B and LLaMA-2-13B (Touvron et al.,

Dataset (→)	MedMCQA		MedQA		MMLU-Med		PubMedQA		BioASQ		MedNLI		MediQA-RQE		PubHealth	
Method (↓)/Metrics (→)	Acc. (%)	Δ (%)	Acc. (%)	Δ (%)	Acc. (%)	Δ (%)	Acc. (%)	Δ (%)	Acc. (%)	Δ (%)	Acc. (%)	Δ (%)	Acc. (%)	Δ (%)	Acc. (%)	Δ (%)
LLaMA-2-7B (2023)	16.00	–	16.42	–	20.13	–	17.00	–	16.13	–	17.80	–	23.91	–	16.89	–
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+SFT	42.86	–	33.39	–	28.22	–	60.80	–	63.31	–	65.52	–	35.42	–	22.00	–
+MedAdapter	**44.85**	+1.99	**40.61**	+7.22	**35.85**	+7.63	**68.00**	+7.20	**66.94**	+3.63	**74.95**	+9.43	**46.54**	+11.12	**33.36**	+11.36
+SFT-LoRA (2022)	28.95	–	23.89	–	24.54	–	55.00	–	50.00	–	25.97	–	32.17	–	20.47	–
+MedAdapter	35.69	+6.74	28.04	+4.15	31.90	+7.36	62.90	+7.90	60.48	+10.48	35.96	+9.99	39.57	+7.40	25.26	+4.79
gpt-3.5-turbo (2022)	49.74	–	61.51	–	59.75	–	56.00	–	84.68	–	66.64	–	50.00	–	23.38	–
+MedAdapter	59.02	+9.28	68.66	+7.15	73.58	+13.83	73.40	+17.40	93.55	+8.87	75.09	+8.45	52.61	+2.61	33.43	+10.05
+Azure-SFT (2023)	61.82	–	63.32	–	70.55	–	71.40	–	95.16	–	91.27	–	58.08	–	36.56	–
+MedAdapter	**65.50**	+3.68	**68.89**	+5.57	**76.73**	+6.18	**77.00**	+5.60	**95.97**	+0.81	**91.42**	+0.15	**59.56**	+1.48	**42.49**	+5.93
+MedRAG (2024)	51.80	–	64.36	–	68.85	–	50.00	–	87.55	–	–	–	–	–	–	–
+MedAdapter	56.20	+4.40	67.16	+2.80	74.86	+6.01	63.00	+13.00	94.42	+6.87	–	–	–	–	–	–

Table 2: Complementary analysis results (accuracy) of combining training- and test-time adaptation for both white- and black-box LLMs on biomedical tasks. **Bold** indicates the best performance within white/black-box LLMs.

2023), demonstrating a generalizable solution for white-box LLM biomedical domain adaptation.

Black-box LLM Adaptation. As expected, black-box LLMs, with their extensive model parameters and large pre-training corpora, significantly outperform white-box LLMs (Table 1) across all biomedical applications. ◇ Effectiveness: We observe that MedAdapter successfully adapts gpt-3.5-turbo (OpenAI, 2022) across all tasks, achieving an average performance improvement of 11.31% for QA, 8.45% for NLI, 2.61% for RQE, and 20.05% for health fact-checking. ◇ Privacy-Preserving: Notably, MedAdapter achieves competitive or even superior performance compared to supervised fine-tuning via Microsoft Azure APIs, without necessitating the sharing of local training samples with third parties. This may be due to the opacity of the fine-tuning service, which only allows access to a very limited number of adjustable parameters within a prescribed range[4], leading to suboptimal fine-tuning performance. ◇ Generalization: We could also extend MedAdapter for more advanced LLMs such as gpt-4 (OpenAI, 2023), demonstrating a flexible and generalizable solution for adapting black-box LLMs in medical reasoning. ◇ Robustness: MedAdapter provides more effective adaptation compared to other privacy-preserving methods, such as self-consistency (Wang et al., 2023b) and MedRAG (Xiong et al., 2024). Specifically, we observe only a slight improvement or even a decrease in performance when adapting RAG-based methods compared to direct adaptations of backbone black-box LLMs. This can be attributed to the conditional generation nature of RAG, which typically results in less diverse candidate solutions.

3.3 MedAdapter Complements Other Adaptation Techniques

In Table 2, we perform a complementary analysis to demonstrate the flexibility of MedAdapter by integrating both train-time and test-time adaptation. For example, in the biomedical QA tasks, MedAdapter yields an additional performance improvement of 5.53% and 4.37% for white-box and black-box LLMs, respectively, over train-time adaptation (*i.e.*, supervised fine-tuning). When combined with train-time adaptation, MedAdapter outperforms either train-time or test-time adaptation alone, demonstrating its utility as a flexible solution that complements existing train-time adaptation methods (*e.g.*, LoRA) (Hu et al., 2022) and even test-time adaptation (*e.g.*, MedRAG) (Xiong et al., 2024) to further boost model performance.

3.4 Cost Estimation

Table 3 compares the cost estimations of different black-box LLM adaptation methods in the main biomedical QA tasks. Compared to the Microsoft OpenAI service, which achieves an average improvement of 10.11% over the backbone LLM, MedAdapter obtains an improvement of 11.31% at only 15.59% of the cost during the fine-tuning stage. This is because MedAdapter relies on inference APIs ($1 per 1M token) to generate candidate solutions, which is significantly less expensive than using fine-tuning APIs ($8 per 1M token). Moreover, customized models accessed through APIs incur 1.58× higher costs during the inference stage than MedAdapter due to the increased prices for input ($3 per 1M tokens) and output ($6 per 1M tokens) usage compared to the original models ($1

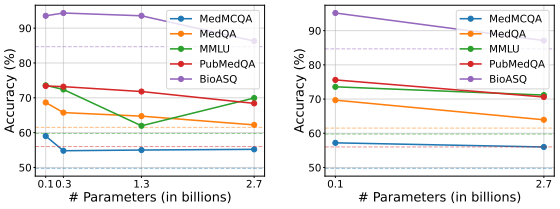
[4]In the Microsoft OpenAI fine-tuning service, users are permitted to modify only four hyperparameters within a limited range: (1) the number of epochs, (2) the batch size, (3) the learning rate multiplier, and (4) the random seed. Details for parameter studies of supervised fine-tuning via Microsoft Azure APIs are available in Appendix D.

Dataset (→)	MedMCQA		MedQA		MMLU-Med		PubMedQA		BioASQ	
Method (↓) / Costs ($)	Training	Inference	Training	Inference	Training	Inference	Training	Inference	Training	Inference
gpt-3.5-turbo (OpenAI, 2022)	–	1.37	–	0.67	–	0.06	–	0.16	–	0.03
+MedAdapter	7.67	10.40	42.57	5.37	3.49	0.44	0.92	1.14	1.41	0.35
+Azure-SFT (Peng et al., 2023)	71.18	10.88	172.85	6.83	38.93	3.18	38.17	3.76	38.48	3.24
+OpenAI-SFT*	23.07	32.87	195.45	16.10	4.01	3.12	15.76	1.34	6.77	1.05

Table 3: Cost ($) estimations of adapting black-box LLMs to biomedical QA tasks based on gpt-35-turbo-1106. ∗ denotes an estimated cost, as the OpenAI-SFT is not compliant with HIPAA regulations.

Dataset (→)	BioASQ		
Method (↓) / Memory (GiB)	Training	Inference	Acc. (%)
LLaMA-2-7B (Touvron et al., 2023)	–	25.42	16.13
+MedAdapter	11.60	33.00	62.90
+SFT-LoRA (Hu et al., 2022)	54.76	34.65	50.00
+SFT	78.65	25.42	63.31

Table 4: GPU memory (GiB) usage estimations of adapting white-box LLMs to biomedical QA tasks.



(a) General LMs. (b) Biomedical LMs.

Figure 3: Scale-up performance on multiple general and biomedical domain-specific language models (LMs) as the base LM of MedAdapter. The dashed line denotes the performance of the base model, gpt-3.5-turbo.

per 1M tokens for input usage and $2 per 1M tokens for output usage).

In addition, we also report an estimated cost through the OpenAI supervised fine-tuning API [5] without implementation due to the conflict with HIPAA compliance, which is significantly higher than MedAdapter in both the fine-tuning and inference stages. Notably, there are differences between the Microsoft Azure OpenAI fine-tuning API service and the OpenAI fine-tuning API: (1) Microsoft Azure service charges based on training hours, including an additional hosting cost for model deployment, and (2) OpenAI fine-tuning API incurs a higher cost per token for both training and inference but does not include additional hosting fees.

3.5 Parameter Efficiency

Table 4 evaluates the GPU memory (GiB) usage of different white-box LLMs adaptation methods, including PEFT methods. Compared to supervised fine-tuning of a LLaMA-2-7B (Touvron et al., 2023), MedAdapter achieves competitive performance while only fine-tuning a 110M-parameter model, using 14.75% of the GPU memory. Compared to other parameter-efficient adaptation methods, such as LoRA (Hu et al., 2022), which updates approximately 170M parameters, MedAdapter demonstrates a 12.90% improvement in model performance while utilizing only 21.18% of the GPU memory. We also observe MedAdapter requires a slightly higher GPU memory usage during the inference stage, as it requires loading the original model. However, this usage remains lower than that required for supervised fine-tuning or LoRA.

3.6 Scale-up Analysis

In Figure 3, we explore the impact of scaling up the base model of MedAdapter from 110M to 2.7B parameters, utilizing both general-domain and biomedical domain-specific language models. Additional model details for the scale-up analysis are available in Appendix E. Interestingly, we observe very limited or no improvement with the increase in model size, potentially due to the following reasons: (1) MedAdapter serves as a scoring function that heavily relies on language comprehension rather than generative capabilities, which is a natural fit to encoder-only model; and (2) the limited fine-tuning data available may allow smaller models to more effectively capture underlying patterns within the candidate solutions. Additionally, domain-specific language models exhibit slightly superior performance, likely due to the integration of more targeted knowledge during their pre-training phase.

3.7 Effect of Learning Objectives

We compare the cross-entropy loss (classification) utilized in MedAdapter with the InfoNCE loss (Oord et al., 2018) and pairwise loss (Stiennon et al., 2020) in Table 5 to empirically study

[5] https://openai.com/pricing

Loss (↓) / Dataset (→)	BioASQ	MMLU	MedMCQA
InfoNCE (Oord et al., 2018)	87.90	69.18	57.43
Pairwise (Stiennon et al., 2020)	92.74	72.33	**59.83**
Cross-entropy (**Ours**)	**93.55**	**73.58**	59.02

Table 5: Comparison of different learning objectives with `gpt-3.5-turbo` as the backbone LLM.

Dataset (↓)	Method (↓)	BLEU	Rouge-1	Rouge-L
MediQA	`gpt-3.5-turbo`	2.697	0.2370	0.1571
	`+MedAdapter`	**3.096**	**0.2464**	**0.1591**
CORD19	`gpt-3.5-turbo`	1.420	0.1672	0.1312
	`+MedAdapter`	**1.739**	**0.1816**	**0.1559**

Table 6: Generalization of `MedAdapter` into medical generative tasks, including open-ended medical QA (MediQA) and clinical text summarization (CORD19).

the effect of different learning objectives. The pairwise loss demonstrates inferior performance compared to the classification loss, especially when the base model performs well. This is due to the limited availability of negative samples, which makes it challenging to construct positive-negative pairs. Conversely, for those with limited base performances, it is relatively easier to sample such pairs during the generation process. In addition, the InfoNCE loss imposes even more demanding prerequisites than the pairwise loss and classification loss. It necessitates the inclusion of one positive sample and multiple negative samples within a single batch. We include additional loss function details in Appendix F.

3.8 Effect of Training Samples

Figure 4 presents the effect of training samples regarding the performance gain. We find that `MedAdapter` is label-efficient, achieving noticeable performance improvements with only 40% to 60% of the training examples (e.g., input-label pairs). Additionally, `MedAdapter` reduces the dependency on costly high-quality reasoning step annotations, particularly valuable in the context of low-resource medical reasoning tasks.

3.9 `MedAdapter` on Generation Tasks

To demonstrate the effectiveness of adapting LLMs for generative tasks, we conduct additional experiments on two medical generative tasks (see Table 6), including open-ended question answering using MediQA (Savery et al., 2020) and text summarization with Medical_CORD19 (Wang et al., 2020). Experimental results demonstrate that

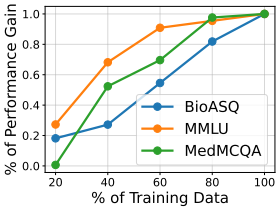


Figure 4: Label Efficiency.

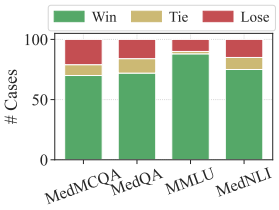


Figure 5: Human Study.

`MedAdapter` successfully improves the black-box LLM `GPT-3.5-turbo` for both tasks, demonstrating its generalizability and effectiveness in domain adaptation for medical generative applications.

3.10 Human Study on Adaptation Score

Following the guideline in Appendix G, we conduct human studies to measure the alignment between adaptation scores generated by `MedAdapter` and human preferences. We randomly select 100 instances from two distinct tasks (QA and NLI) in four datasets (MedMCQA, MedQA, MMLU, and MedNLI) for a thorough evaluation. From Figure 5, we observe that `MedAdapter` achieves a relatively high win rate across multiple datasets, indicating a meaningful adaptation score that aligns with human preferences. We present more case studies with adaptation scores in Appendix H.

4 Related Works

Train-Time Adaptation of LLMs for Biomedical Domains. To enhance the biomedical capabilities of LLMs, prior research has employed large-scale domain-specific corpora to customize white-box LLMs for medical reasoning, including: (1) *Pre-Training*, such as BioGPT (Luo et al., 2022), Meditron (Chen et al., 2023b), Biomistral (Labrak et al., 2024) and BioMedLM (Bolton et al., 2024a); (2) *Fine-Tuning*, such as MedAlpaca (Han et al., 2023), ChatDoctor (Yunxiang et al., 2023), PMC-LLaMA (Wu et al., 2024); and (3) *Parameter-Efficient Fine-Tuning (PEFT)*, such as Clinical LLaMA-LoRA (Gema et al., 2023). Pre-training or fine-tuning LLMs necessitates substantial computational resources, particularly as model sizes continue to increase, which may not be readily accessible to academic or medical researchers (Bolton et al., 2024b). For example, Biomistral (Labrak et al., 2024) requires approximately 5K computing hours of A100 80GB GPU. While PEFT-based adaptation methods (Gema et al., 2023) are more efficient as they only update a small subset of parameters, they might yield suboptimal performance. Al-

ternatively, MedAdapter offers a different test-time solution by leveraging the emerging generative capabilities of LLMs, avoiding exclusive training on large-scale domain-specific data while utilizing significantly fewer model parameters.

Test-Time Adaptation of LLMs. Test-time adaptation involves customizing models to test data that may differ in distribution from the original training data (Liang et al., 2023; Ye et al., 2023). Existing methods for test-time adaptation of LLMs towards medical reasoning include: (1) *Prompting*-based methods, such as Med-PaLM (Nori et al., 2023); and (2) *Retrieval-Augmented Generation (RAG)*-based methods, such as MedRAG (Xiong et al., 2024) and Self-BioRAG (Jeong et al., 2024). MedAdapter introduces a third option for test-time adaptation of LLMs in medical reasoning by training a small adapter to score the candidate solutions generated by large models, thereby eliminating the need for fine-tuning the original LLM while still effectively facilitating target domain adaptation.

5 Conclusion

In this study, we propose MedAdapter to address a unique challenge in adopting LLMs in real-world clinical scenarios with limited computational resources and strict privacy requirements. MedAdapter strikes a balance between effective model adaptation and reasonable computational costs by employing a BERT-sized language model as an adapter to select candidate solutions generated by larger LLMs, thereby obviating the need to fine-tune the entire LLMs. MedAdapter may offer a unified and generalizable practical solution for effectively, privacy-preservingly, cost-effectively, and transparently adapting LLMs to real-world biomedical research and practice.

Limitations

In this work, we propose MedAdapter for test-time adaptation of LLMs in medical reasoning applications. However, we have identified several limitations of MedAdapter: (1) **Access to Label Information**: MedAdapter still requires access to task-specific labeled data to fine-tune a small adapter. This may not be feasible in some real-world scenarios where label information is restricted or unavailable. (2) **On-Device Inference**: In the adaptation of black-box LLMs, the fine-tuning process does not share any data with third parties through APIs; however, it cannot handle queries involving sensitive or patient-identifiable information during the inference stage. Furthermore, the extensive parameters of black-box LLMs post challenges for on-device inference. (3) **Resource Limitations**: Due to restricted access to fine-tuning API services and budget constraints, our experiments with black-box fine-tuning are limited to GPT-3.5-Turbo via the Microsoft Azure fine-tuning API service.

Ethics Statements

In strict adherence to the PhysioNet Credentialed Health Data Use Agreement 1.5.0[6], we expressly forbid the dissemination of confidential patient information to any third party, including via online services such as APIs. To guarantee the responsible utilization of Azure OpenAI Service in accordance with the guideline[7], we have deliberately withdrawn from the human review process by submitting the Azure OpenAI Additional Use Case Form[8]. It effectively precludes third parties from accessing and processing protected health information (PHI) for any purpose. We maintain a rigorous monitoring process to ensure our compliance with these guidelines and pertinent privacy legislation, thereby upholding the highest ethical standards in the use of data throughout our research.

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[7] https://physionet.org/news/post/gpt-responsible-use

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A Dataset Details

We evaluate the domain adaptation capabilities of both white-box and black-box LLMs in medical reasoning tasks using five biomedical QA and three additional biomedical NLP datasets. We have selected these datasets due to their extensive utilization in assessing the language comprehension and reasoning capabilities of LLMs in the medical domain (Bolton et al., 2024a; Xiong et al., 2024; Luo et al., 2023; Jeong et al., 2024). Dataset statistics are available in Table 7.

Dataset	# Train	# Test	Source
MedMCQA (Pal et al., 2022)	3000	4183	Exam
MedQA (Jin et al., 2021)	10178	1273	Exam
MMLU (Hendrycks et al., 2021)	1299	163	Exam
PubMedQA (Jin et al., 2019)	450	500	Literature
BioASQ (Tsatsaronis et al., 2015)	494	124	Literature
MedNLI (Shivade, 2017)	11232	1422	Patient Query
MediQA-RQE (Ben Abacha et al., 2019)	8588	302	Patient Query
PubHealth (Kotonya and Toni, 2020)	9804	1231	Literature

Table 7: Dataset statistics.

A.1 Biomedical QA Dataset Details

MedMCQA. MedMCQA[9] (Pal et al., 2022) is a large-scale and comprehensive dataset for multi-choice (four-option) medical question answering. It is derived from real-world medical entrance exam questions (Indian AIIMS and NEET-PG) and consists of over 194,000 high-quality medical questions. These questions cover 2,400 healthcare topics and 21 medical subjects, exhibiting a wide range of topical diversity. The average token length is 12.77.

[9] https://medmcqa.github.io

MedQA. MedQA[10] (Jin et al., 2021) is a multi-choice question-answering dataset collected from the professional medical board exam, the United States Medical License Exams (USMLE). It comprises 12,723 questions sourced from a comprehensive collection of 18 English medical textbooks that have been extensively utilized by medical students and USMLE candidates. Questions in MedQA cover a wide range of topics in clinical medicine, necessitating responses with professional expertise and complex multi-hop reasoning across multiple pieces of evidence. The average question and option length is 116.6 and 3.5, respectively.

MMLU-Med. MMLU[11] (Hendrycks et al., 2021) is a comprehensive multi-task language understanding test dataset that encompasses 57 tasks across various domains such as mathematics, history, computer science, law, and *etc.* In our experiments, we specifically focus on a subset of seven medical reasoning-related tasks (Singhal et al., 2023), including clinical knowledge, college biology, college medicine, high school biology, medical genetics, professional medicine, and virology.

PubMedQA. PubMedQA[12] (Jin et al., 2019) is a biomedical question and answering dataset derived from PubMed abstracts. It contains 1k expert-annotated multi-choice question-and-answer samples based on 211.3k PubMed articles. The task of PubMedQA is to provide answers to research questions with yes/no/maybe responses based on the corresponding abstracts. The average question and context length is 14.4 and 238.9, respectively.

BioASQ. BioASQ[13] (Tsatsaronis et al., 2015) is a large-scale biomedical semantic indexing and question-answering dataset. It includes tasks related to information retrieval (Task A) and machine reading comprehension (Task B). Similar to PubMedQA (Jin et al., 2019), BioASQ leverages biomedical scientific articles, providing text fragments that serve as the ground truth for machine reading comprehension. Following Xiong et al. (2024), we focus on 618 machine reading comprehension questions (Task B) with binary (yes/no) answers from the most recent five years (from 2019 to 2023). The average token length of each question is 17.

[10] https://github.com/jind11/MedQA
[11] https://github.com/hendrycks/test
[12] https://pubmedqa.github.io
[13] https://github.com/AKSW/BioASQ-AT

A.2 Additional Biomedical Dataset Details

MedNLI. MedNLI[14] (Shivade, 2017) is a collection of natural language inference tasks for ascertaining whether a hypothesis can be deduced from a given premise. It is derived from MIMIC-III and annotated by medical professionals. It comprises 14,049 distinct sentence pairs grounded in the medical history of patients.

MediQA-RQE. MediQA-RQE[15] (Ben Abacha et al., 2019) is a comprehensive compilation of biomedical NLP tasks designed to facilitate the recognition of question entailment. It consists of 8,588 pairs of medical questions, with the primary objective being the identification of entailment between two questions in the context of question answering.

PubHealth. PubHealth[16] (Kotonya and Toni, 2020) is a comprehensive dataset designed for automated fact-checking of public health claims. Each instance in the PUBHEALTH dataset is assigned a veracity label, indicating whether it is *true*, *false*, *unproven*, or a *mixture*. It comprises 11.8K distinct claims related to public health and health policy, obtained from multiple health information websites or news journals.

B Implementation Details

B.1 Additional implementation details

Black-Box LLM Adaptation. For black-box LLM adaptation, `gpt-3.5-turbo` (version 1106) serves as the main backbone LLM. We also adapt `gpt-4` (version 1106) for a comprehensive evaluation. During the evaluation of Azure-SFT, certain questions and answers may be filtered by the Azure content filter to ensure the safety of the content generated. In order to avoid any potential bias caused by these filtered questions, we exclude them from the evaluation process to maintain the integrity of our assessments.

White-Box LLM Adaptation. For white-box LLM adaptation, we leverage `LLaMA-2-7B` as the backbone LLM. During the fine-tuning phase, learning rates are set to $2e-5$ for `MedAdapter` and $2e-4$ for supervised fine-tuning and LoRA (Hu et al., 2022), respectively. The global batch size is

[14] https://jgc128.github.io/mednli/
[15] https://sites.google.com/view/mediqa2019
[16] https://github.com/neemakot/Health-Fact-Checking

maintained at 8 for all white-box adaptation experiments. To maintain the same model size in the case of LoRA, we train the base LLM with $r = 1024$, $\alpha = 2048$, bfloat16 quantization, and DeepSpeed gradient checkpointing (Rasley et al., 2020).

Hardware Details. All experiments are conducted on four NVIDIA A100 GPUs, accommodating a maximum sequence length of 512 tokens.

B.2 Prompt Templates

B.2.1 MedMCQA

The prompting format for MedMCQA dataset is listed as follows:

<MedMCQA> Prompt

```
Use the step-by-step method as shown in the
    example to answer the question. You should
    give the explanation steps and final answer
    based on the provided context.

Example:
Q: What is the most probable poal of entry of
    Aspergillus? (A) Puncture wound, (B) Blood,
    (C) Lungs, (D) Gastrointestinal tract
A: Aspergillus species are widely distributed
    on decaying plants, producing chains of
    conidia.
Aspergillus species unlike Candida species do
    not form the pa of normal flora of humans.
They are ubiquitous in the environment; hence
    transmission of infection is mostly
    exogenous.
Aspergillus transmission occurs by inhalation
    of airborne conidia.
Risk Factors for invasive aspergillosis are:
    Glucocoicoid use (the most impoant risk
    factor) Profound neutropenia or Neutrophil
    dysfunction Underlying pneumonia or COPD,
    tuberculosis or sarcoidosis Antitumor
    necrosis factor therapy.
#### C.

Here is your question. Please respond to this
    question based on the context and by
    adhering to the given format: provide
    step-by-step reasoning (one sentence per
    line), then give the final answer (A/B/C/D)
    after '####'.
```

B.2.2 MedQA

The prompting format for MedQA dataset is listed as follows:

<MedQA> Prompt

```
Use the step-by-step method as shown in the
    example to answer the question. You should
    give the reasoning steps and final answer
    based on the provided context.

Example:
Q: A 21-year-old sexually active male complains
    of fever, pain during urination, and
    inflammation and pain in the right knee. A
    culture of the joint fluid shows a bacteria
    that does not ferment maltose and has no
    polysaccharide capsule. The physician
    orders antibiotic therapy for the patient.
    The mechanism of action of action of the
    medication given blocks cell wall synthesis,
    which of the following was given? (A)
    Gentamicin, (B) Ciprofloxacin, (C)
    Ceftriaxone, (D) Trimethoprim.
A: The symptoms and culture results suggest a
    bacterial infection that affects both the
    urinary tract and joints, indicating a
    systemic infection.
Bacteria that do not ferment maltose and lack a
    polysaccharide capsule could indicate a
    variety of bacteria, but the treatment
    approach focuses on the mechanism of action
    of the antibiotic rather than the specific
    bacteria.
Antibiotics that block cell wall synthesis are
    typically beta-lactams, which include
    penicillins and cephalosporins.
Gentamicin is an aminoglycoside antibiotic,
    which works by inhibiting protein
    synthesis.
Ciprofloxacin is a fluoroquinolone, which works
    by inhibiting bacterial DNA gyrase and
    topoisomerase IV, affecting DNA replication.
Ceftriaxone is a third-generation cephalosporin,
    which works by inhibiting cell wall
    synthesis.
Trimethoprim is an antibiotic that inhibits
    bacterial dihydrofolate reductase,
    affecting folic acid synthesis.
#### C.

Here is your question. Please respond to this
    question based on the context and by
    adhering to the given format: provide
    step-by-step reasoning (one sentence per
    line), then give the final answer (A/B/C/D)
    after '####'.
```

B.2.3 MMLU-Med

The prompting format for MMLU-Med dataset is listed as follows:

<MMLU-Med> Prompt

```
Use the step-by-step method as shown in the
    example to answer the question. You should
    give the reasoning steps and final answer
    based on the provided context.

Example:
Q: What size of cannula would you use in a
    patient who needed a rapid blood
    transfusion (as of 2020 medical knowledge)?
    (A) 18 gauge, (B) 20 gauge, (C) 22 gauge,
    (D) 24 gauge.
A: The gauge of a cannula indicates its
    diameter: the smaller the number, the
    larger the diameter of the cannula.
A larger diameter cannula allows for the rapid
    administration of fluids, including blood.
In emergency situations requiring rapid
    transfusion, a larger cannula is preferred
    to ensure quick delivery of blood to the
    patient.
An 18 gauge cannula is larger than the 20, 22,
    and 24 gauge options and is commonly used
```

```
    for rapid transfusions.
#### A.

Here is your question. Please respond to this
    question based on the context and by
    adhering to the given format: provide
    step-by-step reasoning (one sentence per
    line), then give the final answer (A/B/C/D)
    after '####'.
```

B.2.4 PubMedQA

The prompting format for PubMedQA dataset is listed as follows:

<PubMedQA> Prompt

```
Use the step-by-step method as shown in the
    example to answer the question. You should
    give the reasoning steps and final answer
    based on the provided context.

Example:
Q: Do familiar teammates request and accept
    more backup?
A: Transactive memory theory extends to
    high-stress environments in which members'
    expertise is highly overlapping.
Teammates' shared mental models about one
    another increase the likelihood that they
    will request and accept backup.
#### Yes.

Here is your question. Please respond to this
    question based on the context and by
    adhering to the given format: provide
    step-by-step reasoning (one sentence per
    line), then give the final answer
    (Yes/No/Maybe) after '####'.
```

B.2.5 BioASQ

The prompting format for BioASQ dataset is listed as follows:

<BioASQ> Prompt

```
Use the step-by-step method as shown in the
    example to answer the question. You should
    give the reasoning steps and final answer
    based on the provided context.

Example:
Q: Can losartan reduce brain atrophy in
    Alzheimer's disease?
A: Losartan is primarily used for hypertension
    and may indirectly affect factors
    associated with Alzheimer's disease
    progression.
Despite potential neuroprotective effects, such
    as reducing inflammation and oxidative
    stress, there is limited direct evidence
    linking losartan to reduced brain atrophy
    in Alzheimer's disease.
Clinical trials specifically targeting this
    outcome are necessary to establish a
    definitive effect.
#### no

Here is your question. Please respond to this
    question based on the context and by
    adhering to the given format: provide
    step-by-step reasoning (one sentence per
    line), then give the final answer (yes/no)
    after '####'.
```

B.2.6 MedNLI

The prompting format for MedNLI dataset is listed as follows:

<MedNLI> Prompt

```
Use the step-by-step method as shown in the
    example to deduce the relationship between
    the given two sentences. You should give
    the reasoning steps and final answer based
    on the provided context.

Example:
Sentence A: Labs were notable for Cr 1.7
    (baseline 0.5 per old records) and lactate
    2.4.
Sentence B: Patient has elevated Cr
Answer: Sentence A states that the patient's
    Cr (creatinine) level is 1.7, which is
    higher than the baseline of 0.5 according
    to old records.
Sentence B simply states that the patient has
    elevated Cr.
The information in Sentence A supports the
    claim in Sentence B, making the relationship
    entailment.
#### entailment

Here are the given two sentences. What is the
    relationship between the given two sentences?
    Please answer from [entailment, neutral,
    contradiction]. Please give the answer after
    '####'.
```

B.2.7 MediQA-RQE

The prompting format for MediQA-RQE dataset is listed as follows:

<MediQA-RQE> Prompt

```
Does the provided solution correctly answer the
    question? Please answer from [true, false].
    Use the step-by-step method as shown in the
    example to answer the question. You should
    give the reasoning steps and final answer
    based on the provided context.

Example:
Question: What is High Blood Pressure?
Solution: High Blood Pressure. I know you may
    not answer this but my blood pressure comes
    up at night when I am asleep. I take four
    medicines. I have asked doctors why this
    happens and no one knows. This morning at
    four A.M. It was 164 and I took a clonidine
    to help get it done. It worries me so.
Judge: The provided solution does not correctly
    answer the question "What is High Blood
    Pressure?"
The solution discusses a personal experience
    with high blood pressure and medication but
    does not define or explain what high blood
    pressure is.
A correct answer would define high blood
```

```
    pressure  as a condition in which the force
    of the blood against the artery walls is
    too high, typically considered to be 140/90
    mmHg or higher.
#### false

Here is the question and answer. Please then
    give the final judge (true/false) after
    '####'.
```

B.2.8 PubHealth

The prompting format for PubHealth dataset is listed as follows:

<PubHealth> Prompt

```
Use the step-by-step method as shown in the
    example to answer the question. You
    should give the thought steps and final
    answer based on the provided context.
    Please judge whether the claim is true
    or false.

Example:
Claim: Annual Mammograms May Have More
    False-Positives        October 18, 2011
Judge: This article reports on the results
    of a study of nearly 170,000 women who
    had screening mammograms beginning
    between age 40-59.
The study found that over ten years of
    screening mammograms, over half of the
    women will experience a false-positive
    recall for additional mammography.
In addition, 7%-9% of the women will have a
    biopsy for a suspicious lump which is
    not cancerous.
Both of those percentages decrease if the
    woman is screened every other year
    rather than every year.
Even with biennial mammography, 41% of
    women will experience aÂărecall over 10
    years of mammography.
The studyâĂŹs Principal Investigator
    emphasized that âĂin most cases, a
    recall doesnâĂŹt mean you have cancer.âĂİÂă
She hoped this knowledge would reduce the
    anxiety of women who are recalled.
The story never explained the size of the
    decrease in the number of false positives
    between annual (61.3%) and biennial
    screening (41.6%).
Our first two reviewers were a researcher
    who specializes in health decisions and
    a breast cancer survivor trained in
    evidence by the Natiional Breast Cancer
    CoalitionâĂŹs Project LEAD.
This study is valuable because it helps to
    quantify and compare the harms of annual
    and biennial screening, specifically
    the number of false positives and the
    number of unnecessary biopsies.
Prior to this study, estimates of false
    positive screening mammography rates
    varied widely.
The critical question is whether you can do
    less frequent screening, subject women
    to fewer harms and get similar results
    in terms of detection of âĂearly stageâĂİ
    cancer.
This studyâĂŹs data seems to suggest that
    answer is yes.
#### mixture

Here is the claim. Please then give the final
    judge (true/false/mixture/unproven) after
    '####'.
```

C HIPAA Compliance with API Service

Black-box LLMs have set new standards for SOTA performance on biomedical NLP tasks with their inherent capabilities (Nori et al., 2023). Despite these advancements, there remains potential for improvement in domain-specific applications through domain specialization (Chen et al., 2023a). However, the OpenAI fine-tuning API is not compliant with HIPAA regulations and cannot be used directly for clinical data that contains patient information. While the Microsoft Azure OpenAI fine-tuning API service is HIPAA-compliant, it still poses significant risks when it comes to data sharing through external APIs (Shi et al., 2024) and entails substantial costs for model fine-tuning and deployment. `MedAdapter` offers an alternative approach for adapting black-box LLMs without the use of APIs, thereby greatly enhancing data privacy during training and substantially reducing associated API costs.

D Parameter Studies of Azure-SFT

We conduct parameter studies on fine-tuning GPT-3.5-Turbo using the Microsoft Azure fine-tuning API service, as detailed in Table 8. The training loss curves of the main biomedical QA and additional biomedical tasks are depicted in Figures 6 and 7, respectively. The Azure-SFT service offers only a very limited number of adjustable hyperparameters, such as the learning rate multiplier (LRM) and the number of epochs, which leads to a lack of transparency and results in suboptimal fine-tuning performance (Table 1).

E Base Language Model Details for Scale-up Analysis

Table 9 describes details of the base model of `MedAdapter` in scale-up analysis, ranging from 110M to 2.7B parameters.

F Learning Objectives Details

Pairwise Loss. Similar to a reward model, our proposed `MedAdapter` also assigns a scalar reward

LRM	Epoch	MedMCQA	MedQA	MMLU	PubMedQA	BioASQ	MedNLI	MediQA-RQE	PubHealth
0.1	3	57.87	**63.32**	64.78	**68.80**	95.16	87.06	55.65	**36.56**
1	3	59.69	62.92	**70.55**	68.60	**95.97**	**91.27**	53.27	35.17
0.1	5	**61.82**	60.75	67.48	71.40	91.94	88.11	**58.08**	34.17

Table 8: Grid search of fine-tuning GPT-3.5-Turbo through Microsoft Azure fine-tuning API service. **Bold** denotes the optimal results chosen as a reference for Azure-SFT.

Type	Size	Model
General LM	110M	LongFormer-Base (Beltagy et al., 2020)
General LM	330M	LongFormer-Large (Beltagy et al., 2020)
General LM	1.3B	Phi-1.5 (Li et al., 2023b)
General LM	2.7B	Phi-2 (Li et al., 2023b)
Biomedical LM	110M	Clinical-LongFormer (Li et al., 2022)
Biomedical LM	2.7B	BioMedLM (Bolton et al., 2024a)

Table 9: Details of base language models for scale-up analysis.

value to each response. We can then combine the pairwise loss used in reward models to differentiate between positive and negative samples. We reconstruct the original dataset to be comprised of paired comparisons between two responses generated for the same input or prompt. With the data generated in Section 2.3, given a problem description $\mathbf{x}_i$, we leverage the corresponding ground-truth answer and the generations with the correct answers as positive samples $\mathbf{h}^+ = \mathbf{h} \cap \{\hat{\mathbf{h}}_{i,j} \cdot \mathbb{1}_{(\hat{\mathbf{h}}_{i,j}=\mathbf{h}_i)}\}$, and those generated solutions with incorrect answers as negative samples $\mathbf{h}^- = \{\hat{\mathbf{h}}_{i,j} \cdot \mathbb{1}_{(\hat{\mathbf{h}}_{i,j}\neq\mathbf{h}_i)}\}$. We sample at most k positive-negative pairs for each question. The pairwise learning objective is defined as follows:

$$\begin{aligned}&\mathcal{L}_{\text{pair}}(\mathbf{x}_i, \mathbf{h}_i^+, \mathbf{h}_i^-; \theta)\\&= \log \sigma(r_\theta(\mathbf{h}_i^+) - r_\theta(\mathbf{h}_i^-)),\\&= \log \sigma(r_\theta([\mathbf{x}_i||\hat{\mathbf{s}}_i^+||\hat{\mathbf{y}}_i^+]) - r_\theta([\mathbf{x}_i||\hat{\mathbf{s}}_i^-||\hat{\mathbf{y}}_i^-])).\end{aligned} \tag{6}$$

InfoNCE Loss. InfoNCE Loss extends the original positive-negative pair into the comparison between one positive sample and k negative samples. To optimize towards the ground-truth answers, we set the corresponding ground-truth solution and answer as the positive sample $\mathbf{h}_i^+ = \mathbf{h}_i$ for the given question $\mathbf{x}_i$. Regarding the negative samples, we select all the generated samples from the LLM itself, denoted as $\mathbf{h}i^- = \hat{\mathbf{h}}i, j$. Thus, we can define the InfoNCE loss function as follows:

$$\mathcal{L}_{\text{InfoNCE}} = -\mathbb{E}[\log \frac{r_\theta(\mathbf{h}^+)}{\sum_{\hat{\mathbf{h}}_{i,j}\in\mathbf{h}^-} r_\theta(\hat{\mathbf{h}}_{i.j})}]. \tag{7}$$

G Human Evaluation Guidelines

G.1 Biomedical QA Task

The human guideline for biomedical QA tasks is listed as follows:

<Human Evaluation QA> Guideline

```
The goal of this evaluation task is to assess
the given task input, ground-truth answer, and
a pair of reasoning solutions from the LLM.
Your objective is to determine which reasoning
the solution will ultimately yield the correct
ground-truth answer for that input. For all
biomedical QA datasets, your responsibility is
to provide a response to each question using
either 'True' or 'False'.
```

G.2 Biomedical NLI Task

The human guideline for biomedical NLI tasks is listed as follows:

<Human Evaluation NLI> Guideline

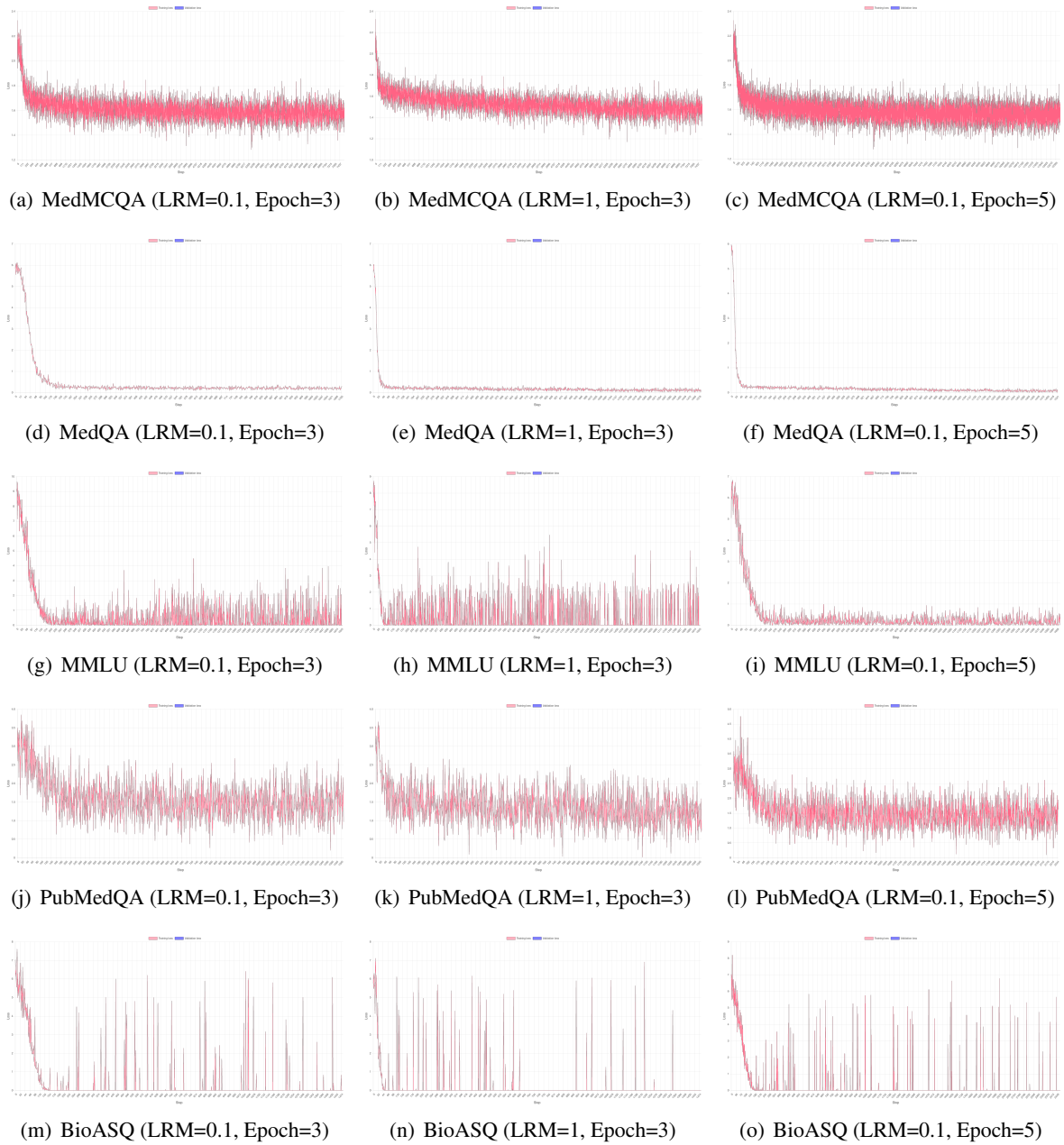
```
The goal of this evaluation task is to assess
the given task input, ground-truth answer, and
a pair of reasoning solutions from the LLM.
Your objective is to determine which reasoning
the solution will ultimately yield the correct
ground-truth answer for that input. For the
biomedical NLI datasets, your responsibility
is to provide a response to predict if the
hypothesis is entailed/neutral/contradicts
the premise.
```

G.3 "Win-Tie-Lose" Judge

For each instance, we randomly sample two generated solutions, e_1, e_2, from eight candidates, with one from the top four (positive) and the other one from the bottom four scores (negative). We then compare `MedAdapter` with human raters by asking four humans to determine which candidate reasoning solution is better, using c_i $(i = 1, 2)$ to denote the number of raters that select e_i. We denote the adaptation scores based on `MedAdapter` as (s_{e_1}, s_{e_2}). The final "Win-Tie-Lose" judgment is determined as follows: (1) **Win**: if $(c_1 > c_2$ and $s_{e_1} > s_{e_2})$ or $(c_1 < c_2$ and $s_{e_1} < s_{e_2})$; (2) **Tie**: if $c_1 = c_2$; and (3) **Lose**: if $(c_1 < c_2$ and $s_{e_1} > s_{e_2})$ or $(c_1 > c_2$ and $s_{e_1} < s_{e_2})$. A higher win rate indicates a greater level of alignment with human preference.

H Case Study of Adaptation Scores

Table 10 gives an example of `MedAdapter` on MMLU dataset. Given the question displayed in the figure, the original self-consistency method selects the most commonly-seen answer "D" as the final answer. Via going through all the training data, the adapter is able to select the most adapted answer from all the candidates and avoid factual errors. For example, generation 4 makes an error regarding the frequency for testing vibration sense and the low score (0.143) is reflective of this mistake. For generations 2, 6, and 7, the solutions provide accurate information but arrive at the wrong conclusion. The high scores (0.767, 0.777, 0.754) reflect the correctness of the reasoning but not the final answer. With the guidance of the `MedAdapter`, we finally select "B", which is accurate and concludes with the correct answer.



(a) MedMCQA (LRM=0.1, Epoch=3) (b) MedMCQA (LRM=1, Epoch=3) (c) MedMCQA (LRM=0.1, Epoch=5)

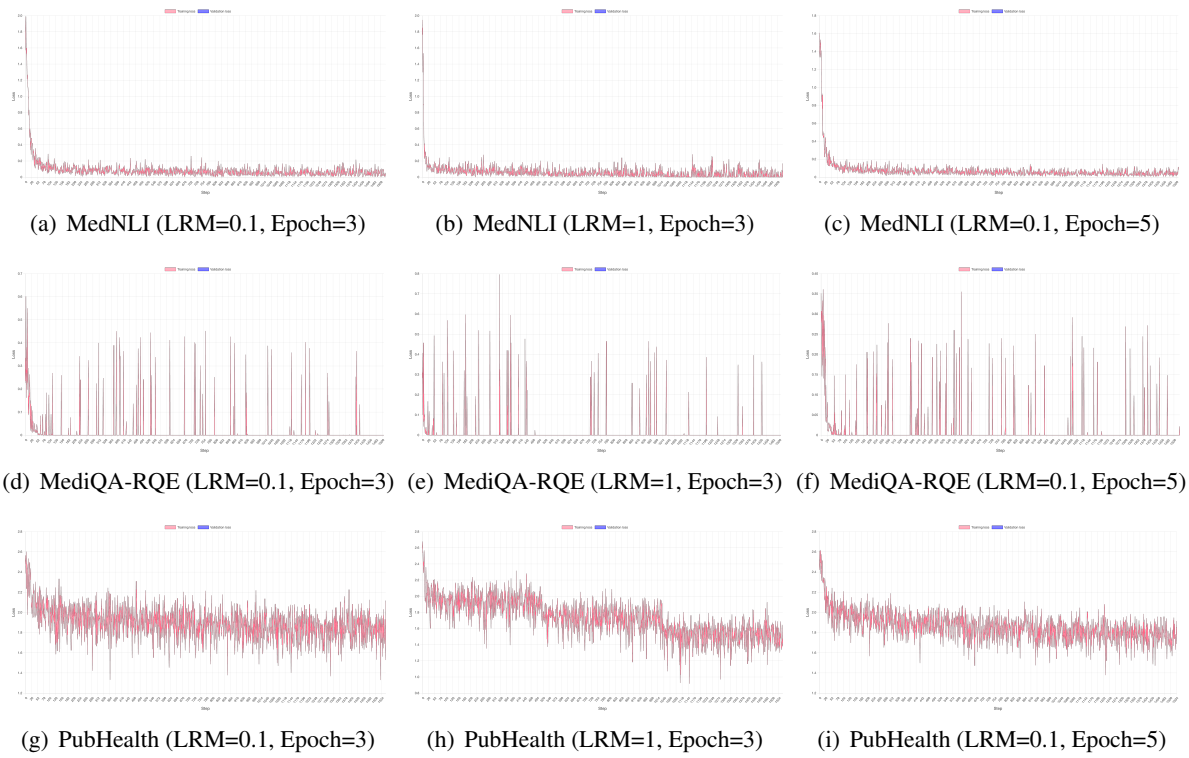
(d) MedQA (LRM=0.1, Epoch=3) (e) MedQA (LRM=1, Epoch=3) (f) MedQA (LRM=0.1, Epoch=5)

(g) MMLU (LRM=0.1, Epoch=3) (h) MMLU (LRM=1, Epoch=3) (i) MMLU (LRM=0.1, Epoch=5)

(j) PubMedQA (LRM=0.1, Epoch=3) (k) PubMedQA (LRM=1, Epoch=3) (l) PubMedQA (LRM=0.1, Epoch=5)

(m) BioASQ (LRM=0.1, Epoch=3) (n) BioASQ (LRM=1, Epoch=3) (o) BioASQ (LRM=0.1, Epoch=5)

Figure 6: Loss function curve of fine-tuning GPT-3.5-Turbo for biomedical QA tasks through Microsoft Azure fine-tuning API service.



(a) MedNLI (LRM=0.1, Epoch=3) (b) MedNLI (LRM=1, Epoch=3) (c) MedNLI (LRM=0.1, Epoch=5)

(d) MediQA-RQE (LRM=0.1, Epoch=3) (e) MediQA-RQE (LRM=1, Epoch=3) (f) MediQA-RQE (LRM=0.1, Epoch=5)

(g) PubHealth (LRM=0.1, Epoch=3) (h) PubHealth (LRM=1, Epoch=3) (i) PubHealth (LRM=0.1, Epoch=5)

Figure 7: Loss function curve of fine-tuning GPT-3.5-Turbo for other biomedical tasks through Microsoft Azure fine-tuning API service.

Table 10: Case study for MedAdapter on MMLU Dataset.

Question: Which of the following is true in a sensory assessment of the arm? (A) It is acceptable to test pain with a venepuncture needle, (B) Proprioception is appreciated via the same tracts as light touch, (C) It is best to test vibration sense with a 256 Hz tuning fork, (D) Impulses for pain travel principally up the dorsal columns **Ground-Truth Answer**: B; **Self-Consistency**: D.	
Generation 1: The sensory assessment of the arm includes testing for pain, proprioception, light touch, and vibration sense. To test pain, a venepuncture needle is not acceptable as it can cause injury and is not a standardized method for pain assessment. Proprioception is appreciated via the dorsal columns, distinct from the tracts for light touch. Vibration sense is best tested with a 128 Hz tuning fork, not a 256 Hz tuning fork. Impulses for pain travel principally up the anterolateral system, not the dorsal columns. #### A. **Prediction 1**: A	Score 1: 0.318
Generation 2: Sensory assessment of the arm involves testing different types of sensation, including pain, proprioception, light touch, and vibration. It is not acceptable to test pain with a venepuncture needle as it can cause tissue damage and is not a standardized method of assessment. Proprioception is appreciated through the dorsal columns, while light touch is appreciated through the spinothalamic tracts, so they are not via the same tracts. Vibration sense is best tested with a 128 Hz tuning fork, not a 256 Hz tuning fork.Impulses for pain travel principally up the spinothalamic tracts, not the dorsal columns. Therefore, the correct answer is (D) Impulses for pain travel principally up the dorsal columns. #### D. **Prediction 2**: D	Score 2: 0.767
Generation 3: Sensory assessment of the arm involves testing different modalities such as pain, proprioception, light touch, and vibration. Pain testing should be performed using a sharp object or pinprick, not a venepuncture needle. Proprioception is appreciated via the dorsal column-medial lemniscal pathway, which is different from the pathway for light touch. Vibration sense is best tested with a 128 Hz tuning fork, not a 256 Hz tuning fork. Impulses for pain travel primarily up the anterolateral system, not the dorsal columns. (D) Impulses for pain travel principally up the dorsal columns. **Prediction 3**: D	Score 3: 0.366
Solution 4: In sensory assessment of the arm, pain is typically tested using a sharp object or pinprick to assess the integrity of small, myelinated (A-delta) and unmyelinated (C) fibers. Proprioception, or the awareness of joint position, is appreciated via the dorsal columns of the spinal cord, which are different from the tracts for light touch. Vibration sense is best tested with a 256 Hz tuning fork, as this frequency is most commonly used for assessing vibration perception. Impulses for pain travel principally up the anterolateral (spinothalamic) tracts, not the dorsal columns. #### A. **Prediction 4**: A	Score 4: 0.143
Explanation 5: Sensory assessment of the arm involves evaluating various sensations such as pain, proprioception, touch, and vibration. It is not acceptable to test pain with a venepuncture needle as it may cause unnecessary discomfort and potential harm to the patient. Proprioception, the sense of the relative position of one's own parts of the body and strength of effort being employed in movement, is appreciated via the dorsal columns of the spinal cord. Light touch and proprioception are appreciated via the same tracts, specifically the dorsal column-medial lemniscal pathway. It is best to test vibration sense with a 256 Hz tuning fork as it is known to be the most effective frequency for testing vibration sense. Impulses for pain travel principally up the anterolateral pathways, specifically the spinothalamic tract. #### A. **Prediction 5**: A	Score 5: 0.301
Explanation 6: In a sensory assessment of the arm, pain should not be tested with a venepuncture needle as it may cause unnecessary harm. Proprioception is appreciated via the dorsal column-medial lemniscal pathway, different from the pathway for light touch. Vibration sense is best tested with a 128 Hz tuning fork, not a 256 Hz tuning fork. Impulses for pain travel principally up the anterolateral system, not the dorsal columns. #### D. **Prediction 6**: D	Score 6: 0.777
Explanation 7: The sensory assessment of the arm involves testing for different modalities of sensation, such as pain, proprioception, light touch, and vibration. It is not acceptable to test pain with a venepuncture needle as it could cause unnecessary discomfort and potential harm to the patient. Proprioception is appreciated via the dorsal column-medial lemniscal pathway, which is different from the pathway for light touch. Vibration sense is best tested with a 128 Hz tuning fork, not 256 Hz tuning fork, as the former is the standard frequency for this assessment. Impulses for pain travel principally up the anterolateral system, not the dorsal columns. Therefore, the correct statement is (D) Impulses for pain travel principally up the dorsal columns. #### D. **Prediction 7**: D	Score 7: 0.754
Explanation 8: Sensory assessment of the arm involves testing for pain, temperature, light touch, proprioception, and vibration. To test pain, a blunt object or pinprick is used instead of a venepuncture needle to prevent injury to the patient. Proprioception is appreciated via the dorsal columns, while light touch is appreciated via the spinothalamic tracts. Vibration sense is best tested with a 128 Hz tuning fork, not 256 Hz. Impulses for pain travel principally up the spinothalamic tracts, not the dorsal columns. #### B. (B) Proprioception is appreciated via the same tracts as light touch. **Prediction 8**: B	**Score 8: 0.896**